MALARIA

DIAGNOSIS AND TREATMENT



MALARIA RESEARCH CENTRE
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- Malaria is a febrile illness caused by parasites of genus *Plasmodium*. It should be treated promptly as negligence may result in serious consequences.

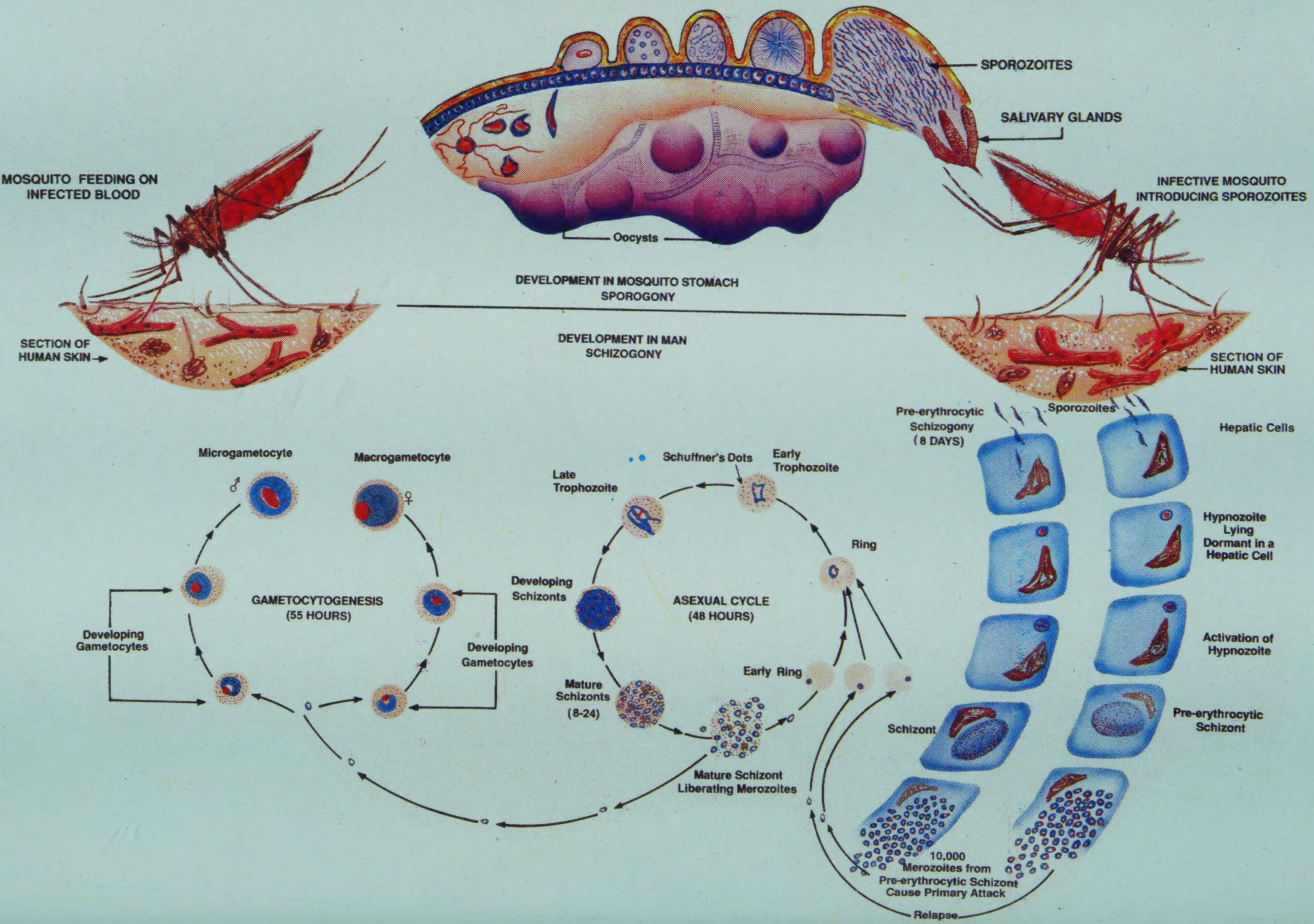
- Malaria is a curable disease without any long-term after effects except in some cases.

- In India malaria transmission does not occur in areas above 6000 ft and some of the coastal areas. This is because malaria carrying mosquitoes are either not present in the coastal rural areas or the temperatures are low so that the parasite development is arrested within the body of the mosquito. All other areas have some degree of risk of contracting malaria, some have more and other less.

- *P. falciparum* malaria is more common in northeastern states, Orissa, forested areas and high humidity areas. But *P. falciparum* cases are found in almost all areas of the country. *P. vivax* is more common in peninsular India where dry conditions prevail. *P. malaríae* is found in small proportions in some parts of India with high humidity and degraded forests like in Orissa.

- Human malaria is caused by four distinct species of *Plasmodium*. In India three predominant infections are:

    - *Plasmodium vivax* (approx. 65%)
    - *Plasmodium falciparum* (35%)
    - *Plasmodium malariae* (<1% restricted distribution)
    - *Plasmodium ovale* (occurs in Africa)


SPOROZOITES
SALIVARY GLANDS
MOSQUITO FEEDING ON INFECTED BLOOD
INFECTIVE MOSQUITO INTRODUCING SPOROZOITES
Oocysts
DEVELOPMENT IN MOSQUITO STOMACH
SPOROGONY
DEVELOPMENT IN MAN
SCHIZOGONY
SECTION OF HUMAN SKIN
SECTION OF HUMAN SKIN
Sporozoites
Pre-erythrocytic Schizogony (8 DAYS)
Hepatic Cells
Hypnozoite Lying Dormant in a Hepatic Cell
Activation of Hypnozoite
Pre-erythrocytic Schizont
Schizont
10,000 Merozoites from Pre-erythrocytic Schizont Cause Primary Attack
Relapse
Microgametocyte
Macrogametocyte
Schuffner's Dots
Early Trophozoite
Late Trophozoite
Ring
Developing Schizonts
ASEXUAL CYCLE
(48 HOURS)
Early Ring
Mature Schizonts
(8-24)
Mature Schizont Liberating Merozoites
GAMETOCYTOGENESIS
(55 HOURS)
Developing Gametocytes
Developing Gametocytes

LIFE CYCLE OF THE PARASITE

- Infection begins when female anopheline mosquito inoculates plasmodial sporozoites from its salivary gland during a blood meal.

- These small motile forms are carried rapidly through blood stream to the liver where they invade hepatic parenchymal cell and a single sporozoite eventually produces several thousand merozoites.

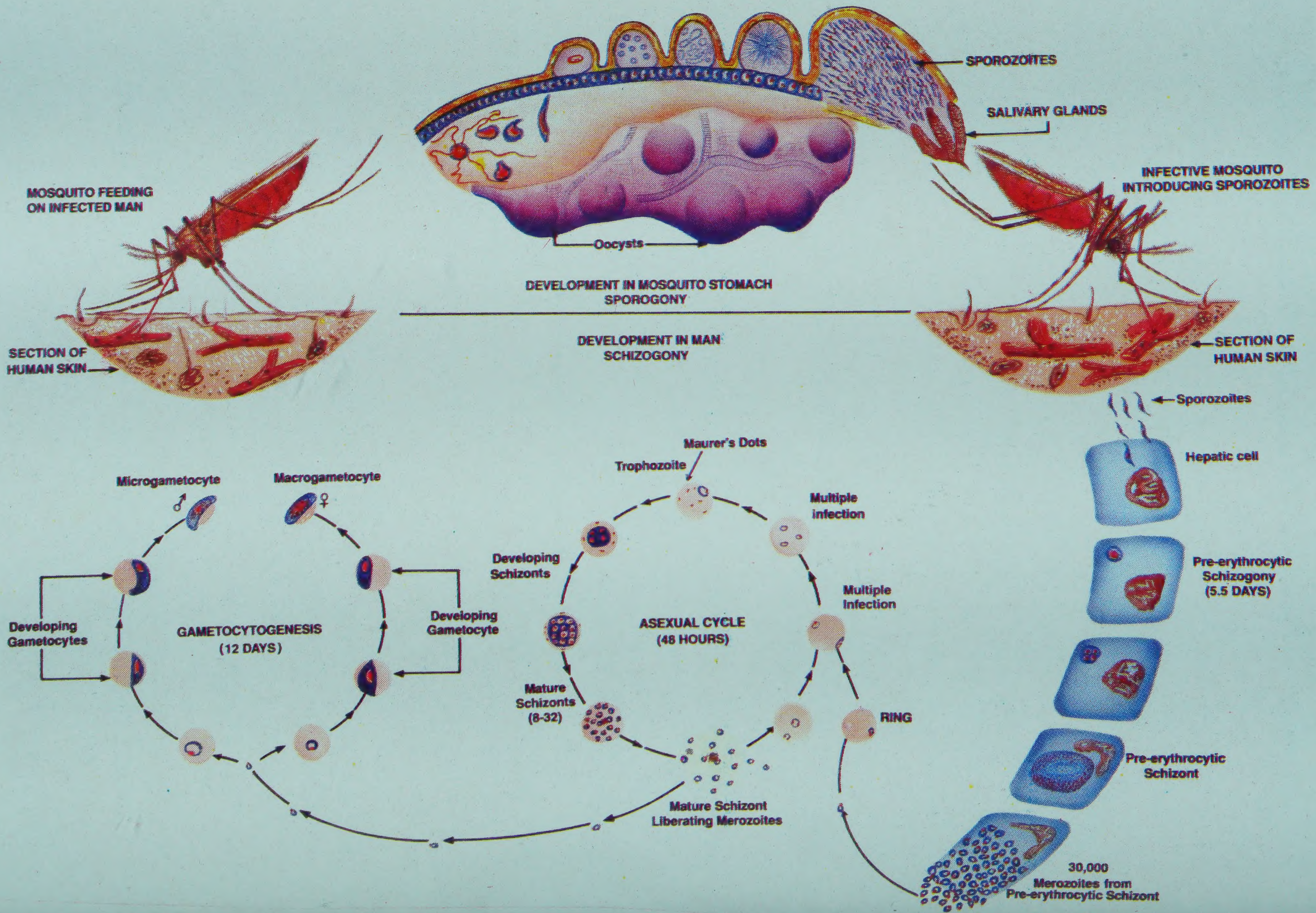
- Swollen liver cell eventually bursts discharging merozoites into blood beginning the symptomatic blood stage of infection.

- In *P.vivax* infections few intrahepatic forms do not divide immediately but remain dormant for months before reproduction begins. These hypnozoites are the cause of relapses in these species.

- After entry into blood stream merozoites rapidly invade erythrocytes and develop into ring, trophozoite and schizont stages. Some of the parasites develop into sexual forms or gametocytes.

- The gametocytes are taken up by female anopheline mosquito on biting a malaria patient. They fuse to form an ookinite which penetrates and encysts in the mosquito gut wall.

- The resulting oocyst expands and bursts to liberate motile sporozoites which then migrate to salivary gland and thus completing the cycle.



Life-cycle of *P. falciparum*

SYMPTOMS

INCUBATION PERIOD

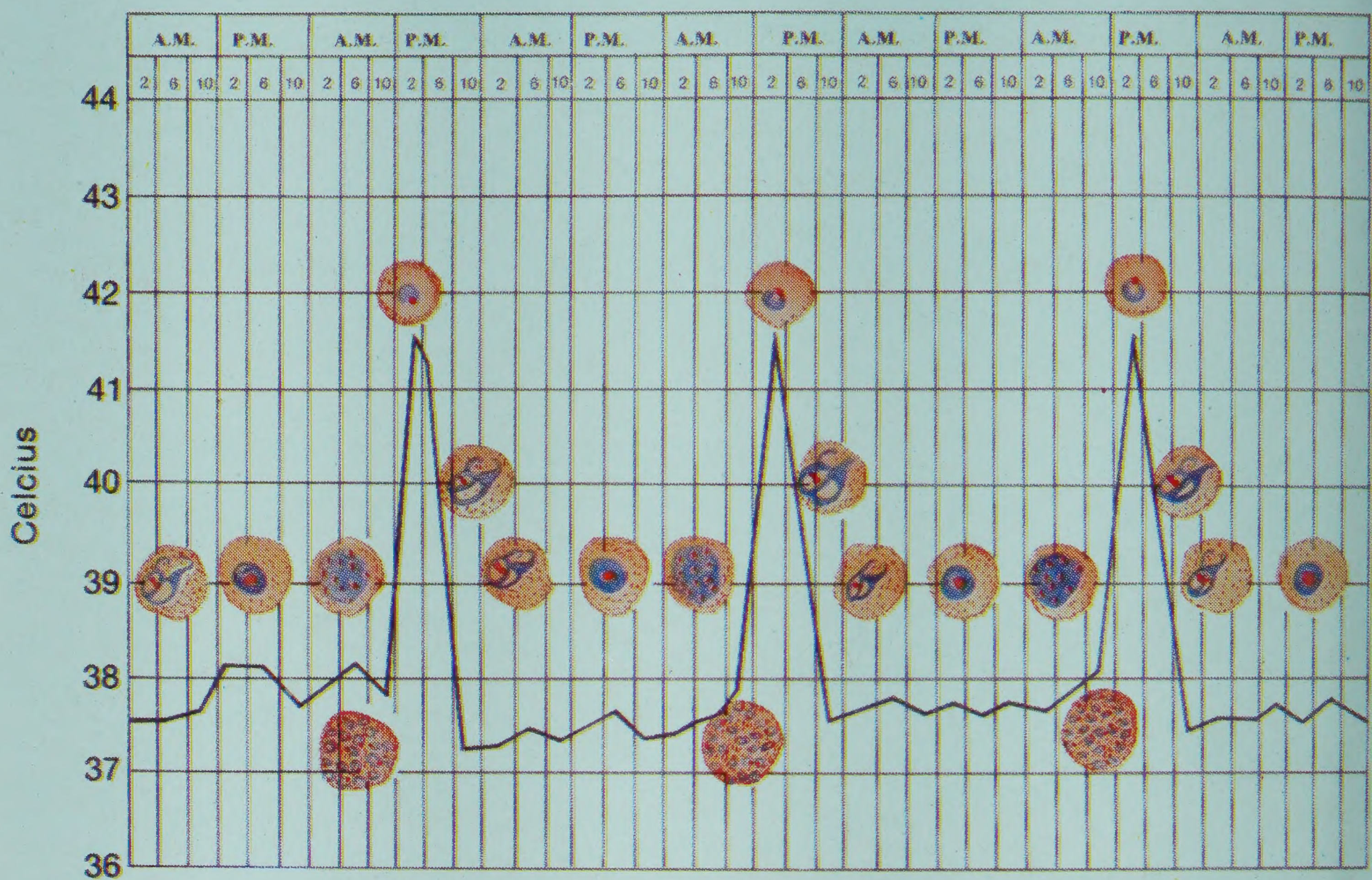
- Incubation period is the interval between infective mosquito bite and first appearance of clinical symptoms/signs.
- Duration of incubation period varies with species. Given below is the average number of days (range) for each species.

P. vivax	-	14 (8-17)
P. falciparum	-	12 (9-14)
P. malariae	-	28 (18-40)
P. ovale	-	17 (16-18)

CLINICAL FEATURES

- There aren't any fully dependable diagnostic clinical features except for regular paroxysms of fever.
- Prodromal symptoms occur before first malarial paroxysm. These are malaise, fatigue, lassitude, headache, dizziness, bodyache, anorexia, nausea and vomiting.
- Malaria causes acute febrile illness which may be characterised by periodic febrile paroxysms occurring every 48 h (alternate day in *P. vivax* and *P. falciparum*) and 72 h (*P. malariae*), with afebrile asymptomatic intervals. However classical periodicity develops only if patient is untreated. In *P. falciparum* spiking fever or daily febrile paroxysm is also common.

Fever periodicity in malaria infection



Fever with tertian periodicity in vivax malaria.

A.M. P.M.

2 6 10

44
43
42
41
40
39
38
37
36

Celcius

CAPILLARY OF INTERNAL ORGAN

Fever with tertian periodicity in falciparum malaria.

- Patient looks ill, may be anaemic or mildly jaundiced with tender enlargement of liver and spleen.

INFLUENCE OF HOST FACTORS

- Severity and course of attack depends on age of the patient, genetic constitution, state of immunity, general health and nutritional status of the patient
- The disease tends to be severe in children, non-immunes and pregnant women
- During pregnancy malaria may cause (especially primigravida)
    - Miscarriage/Abortion
    - Low birth weight due to intra-uterine growth retardation
    - Premature delivery leading to infant mortality
    - Chronic anaemia

SYMPTOMATOLOGY SPECIFIC TO PARASITE SPECIES

- In *P. vivax* symptoms are milder and more regularly divided into hot and cold stage. Short-term or long-term relapses occur due to persistence of hypnozoites in liver.
- In *P. falciparum* infections, headache, nausea and vomiting are more severe than *P.vivax* and there is greater tendency towards development of delirium;

haemolytic jaundice and anaemia. In persons with poor immunity or if treatment is delayed fatal complications may develop.

- *P. malariae* infections resemble those of *P. vivax* but cycle is of 72 h instead of 48 h. Tendency for long-term relapses is marked.
- In *P. ovale*, symptoms are milder than *P. vivax* and cease after few paroxysms even if no treatment is given.

RELAPSE AND RECRUDESCENCES

- Relapses of *P. vivax* and *P. ovale* result from reactivation of hypnozoite forms of parasite in liver.
- Recrudescences of *P. falciparum* and *P. malariae* result from exacerbations of persistent undetectable parasitaemias. Most common cause in *P. falciparum* is treatment failure or drug-resistance.

TREATMENT OF MALARIA

ADVICE

- Contact nearest doctor/PHC and get blood test done for malaria.

SUPPORTIVE THERAPY

- To control pyrexia paracetamol (0.5-1 gm) should be given every 4-6 hours.
- Tepid water sponging in case of high fever.

PRESUMPTIVE TREATMENT (PT)

- Treatment given to all fever cases or cases with history of fever immediately after blood smear collection.
- Chloroquine is the drug of choice

Low risk areas

Dose of chloroquine	:	600 mg (base) (4 tablets) OR 10 mg /kg (base)

High risk areas

Dose of chloroquine	:	1500 mg (base) (10 tablets) OR 25 mg/kg
Day 1 and 2	:	10 mg/kg
Day 3	:	5 mg/kg + Primaquine 0.75 mg/kg

Areas with *P. falciparum*-resistant strains

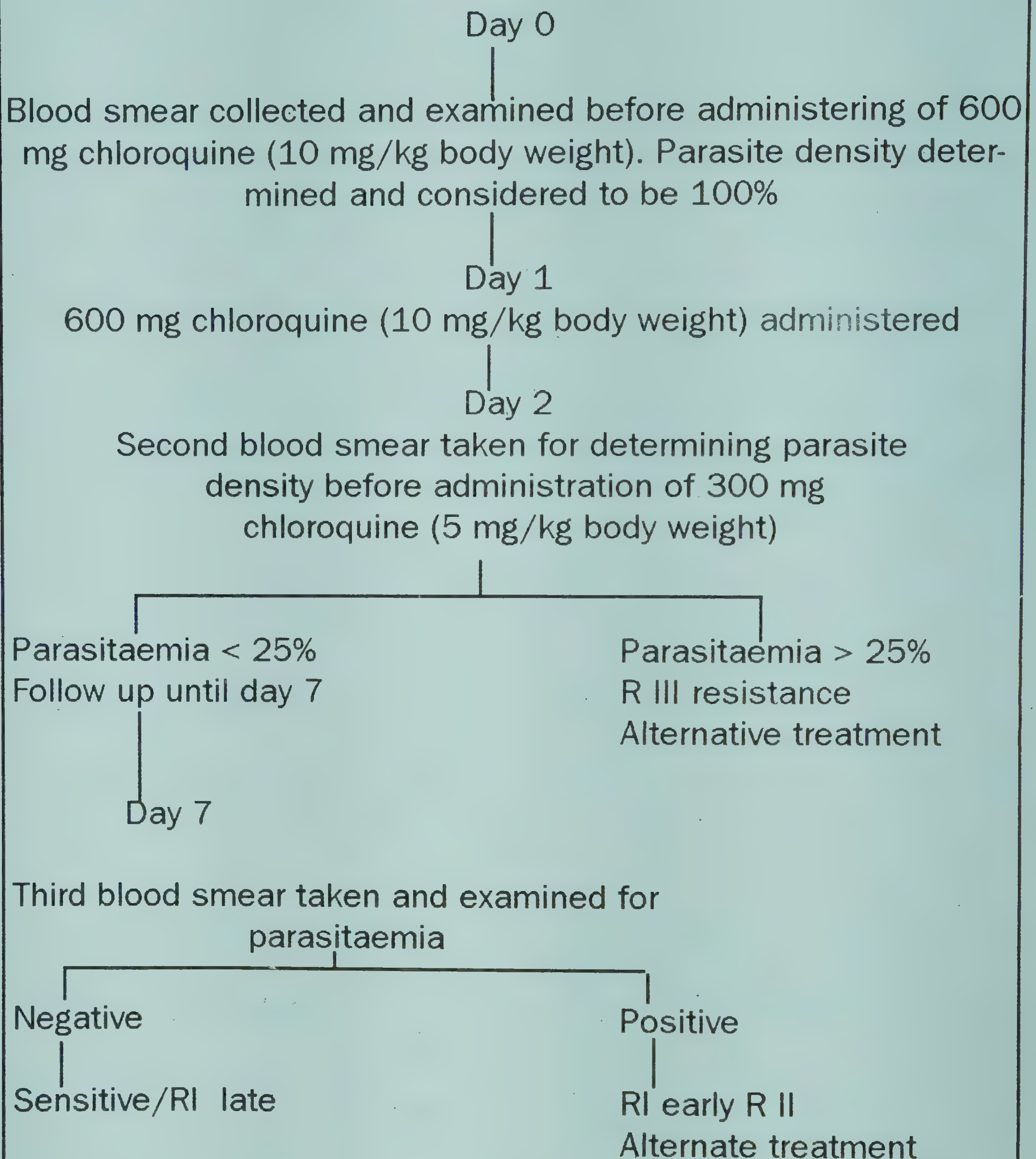
• Chloroquine	:	1500 mg (base) over 3 days +
• Sulfa-pyrimethamine	:	1500 mg + 75 mg (3 Tablets)

Chloroquine is for *P. vivax* and Sulfa-pyrimethamine for resistant *P. falciparum* cases.

RADICAL TREATMENT (RT)

• *P. vivax**	:	Chloroquine 600 mg (base) + Primaquine 15 mg daily x 5 days

SIMPLIFIED IN VIVO TEST SYSTEM FOR DETECTING CHLOROQUINE RESISTANCE IN *P.FALCIPARUM*



- *P. falciparum* * : Chloroquine 1500 mg (base) over 3 days
  +
  45 mg primaquine

- In cases of treatment failure or resistance to chloroquine and sulfa-pyrimethamine, 600 mg quinine 8 hourly for 7 days should be used in combination with tetracycline in the dose of 250 mg/6 hourly or doxicycline 100 mg daily for 7 days.

* In areas where 1500 mg chloroquine and 45 mg primaquine is given as PT there is no need to give RT for *P. falciparum* and only 15 mg primaquine for 5 days is administered for *P. vivax*.

TREATMENT: SPECIAL CONSIDERATIONS IN PREGNANCY

- Even uncomplicated malaria should be treated as an emergency.
- Very effective treatment with lowest possible risk of clinical failure should be given.



- Quinine (not sulfa-pyrimethamine) is the second alternative in chloroquine-resistant cases.
- Sulfa-pyrimethamine can be given in usual dose in second trimester but should be avoided during first trimester and just before delivery.
- Primaquine, tetracycline and doxicycline should not be given throughout pregnancy. In case of *P. vivax* infections, weekly chloroquine can be given to prevent relapse till delivery after which primaquine may be administered.

PREVENTION

A. AVOID INFECTION

- Risk of infective mosquito bites can be reduced by insect proofing and sleeping under mosquito nets, preferably impregnated with pyrethroid insecticides.



B. CHEMOPROPHYLAXIS

- Recommended only for special groups like :
  - Pregnant women
  - Non-immune travellers
  - Service personnel posted in endemic areas

- Effective chemoprophylaxis during second and third trimester of pregnancy reduces the impact of malaria on low birth weight and associated perinatal and post-natal complications.
- Chloroquine base 300 mg weekly is the safe and effective regimen (Start 2 weeks before and continue 4 weeks after leaving endemic area). Proguanil 100-200 mg daily can be added to above regimen in areas of chloroquine resistance.
- The other alternative is doxicycline 100 mg daily, to be started one day before exposure and continued for 4 weeks after leaving the area. The drug is contraindicated in pregnancy.

NEW ANTIMALARIAL DRUGS

- Mefloquine should be used only for multidrug-resistant *P. falciparum* and is not required for *P. vivax*. It is contraindicated in first trimester of pregnancy and should not be used for prophylaxis during pregnancy.
- Artemisinin derivatives are useful for treatment of multidrug-resistant and complicated malaria and should not be used for prophylaxis. They could be used in pregnancy after evaluating risk benefit ratio.

DO'S

- Always prepare peripheral blood smear before administration of antimalarials and treat according to species and stage of parasite present.
- In case clinical condition demands, drug could be administered without waiting for report.
- Administer alternative drugs only after evaluating parasitological and clinical recovery at 48 h.
- Do not treat *P. vivax* infections with Sulfa-pyrimethamine.
- Always give full dose of antimalarials (chloroquine/quinine) in pregnancy.
- Supportive therapy with antipyretics is essential.
- Always administer drugs parenterally (quinine or chloroquine) in severe complicated malaria.
- Primaquine has no role in clinical cure, therefore it can also be given after recovery from acute attack.

DON'TS

- Do not administer chloroquine/quinine on empty stomach.
- Do not give tetracycline/primaquine during pregnancy.
- Never use amodiaquine, sulfadoxine or sulfalene/ pyrimethamine for chemoprophylaxis.
- Do not label malaria as drug-resistant if only mature gametocytes of *P. falciparum* persist in the blood smear after antimalarial therapy.

MALARIA RESEARCH CENTRE

OTHER PUBLICATIONS

(1) Proceedings of the ICMR/WHO Workshop on *Community Participation for Disease Vector Control* (1986) pp. 256
Edited by ***V.P. Sharma***

(2) *Seroepidemiology of Human Malaria — A multicentric study* (1989), pp. 206

Edited by ***V.P. Sharma***

(3) *Indigenous Larvivorous Fishes of India* (1991), pp. 66

A.G.K. Menon

(4) Proceedings of an Informal Consultative meeting WHO/MRC on *Forest Malaria in Southeast Asia* (1991), pp. 206

Editors ***V.P. Sharma*** *and* ***A.V. Kondrashin***

(5) *Malaria Patrika* quaterly (Hindi) 1993 onwards.

(6) Community Participation in Malaria Control (1993), pp. 295

Edited by ***V.P. Sharma***

(7) Larvivorous Fishes of Inland Ecosystem: Proceedings of the MRC-CICFRI Workshop (1994), pp. 224
Editors ***V.P. Sharma*** *and* ***Apurba Ghosh***

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MALARIA RESEARCH CENTRE

The Malaria Research Centre (MRC) was established in the year 1977. Its primary task was to find short-term as well as long-term solutions to the problem of malaria through basic, applied and field operational research. The Centre is currently doing work in the areas of vector biology and control, genetics, cellular and molecular biology, parasitology, epidemiology, pharmacology and biochemistry, that is related to malariology and the development of malaria control strategies. A network of field laboratories in endemic areas provides the testing ground for new technologies and innovative approaches, and helps in the transfer of technology through training, field demonstrations and mass awareness programmes involving various media. The Centre also provides young scientists the opportunity to participate in advanced research through a fellowship programme. Close links in the form of scientific collaborations are maintained with WHO, NMEP and also leading national laboratories. Research findings of the Centre are published in reputed journals. Apart from this, the Centre publishes several books, monographs, proceedings including the Indian Journal of Malariology.